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EXAMINER	
FORD, VANESSA L	

ART UNIT	PAPER NUMBER
1645	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/773,785	FINZI, ERIC	
	Examiner	Art Unit	
	VANESSA L. FORD	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 January 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-8,12-21,23 and 24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4-8,12-21,23 and 24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *06 February 2004* is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

FINAL ACTION

1. This action is in response to Applicant's amendment and remarks filed January 2, 2009. Claims 6-7 and 14-15 have been amended. Claims 2-3, 9-11 and 22 have been canceled. Claims 1, 4-8, 14-21 and 23-24 are under examination.

2. The Declarations filed under 37 CFR 1.132 filed August 18, 2008 and January 2, 2009 are acknowledged. The Declarations of Dr. Bruce P. Capehart and Dr. Eric Finzi under 37 CFR 1.132 filed August 18, 2008 as well as the Declaration of Dr. Eric Finzi filed January 2, 2009 are insufficient to overcome the rejection of claims 1, 4-8, 12-21 and 23-24 as set forth in the last Office action.

Rejections Maintained

3. The rejection of claims 1, 4-8, 12-15 and 23 -24 under 35 U.S.C. 103(a) is maintained for the reasons set forth on pages 2-11, paragraph 3 of the previous Office Action.

The rejection is reiterated below:

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The claims are rejected under 35 U.S.C. 103(a) as unpatentable over Jahanshahi et al *(Journal of Neurology, Neurosurgery and Psychiatry (1992, 55:229-231)* in view of Binder *(U.S. Patent No. 5,714, 468 published February 3, 1998)* and further in view of Carruthers et al *(U.S. Patent No. 6,358, 917 B1, published March 19, 2002)*.

The claims are directed to a method of treating major depression or dysthymia in subject comprising selecting subject diagnosed with major depression or dysthymia using specific clinical criteria for major depression or dysthymia and administering to the subject with major depression or dysthymia a therapeutically effective amount of a neurotoxin to a corrugator supercilii or procerus muscle to cause paralysis of the corrugator supercilii or procerus ,thereby decreasing the ability of the subject to frown and treating major depression or dysthymia in the subject.

Jahanshahi et al teach a method of treating patients suffering from depression (e.g. psychological functioning) before and after administration of botulinum toxin (see the Title and the Abstract). Jahanshahi et al teach that depression can result from primary central neurotransmitter dysfunction (page 229). Jahanshahi et al teach that in this study there was a significant improvement in depression of patients that received botulinum toxin injections (page 231). Jahanshahi et al suggest that use of other concepts or techniques may be help with direct management of psychological aspects, body concept and low self-esteem (page 231). Jahanshahi et al that depression may constitute a reaction to the postural abnormality of the head (page 239).

Jahanshahi et al do not teach administering botulinum toxin to a facial muscle such as a frontalis muscle, an orbicularis oculi muscle, procerus muscle, a corrugator supercilli muscle or depressor anguli oris muscle.

Binder teaches that botulinum toxin can be administered to various muscles in the face and head including the frontalis, orbicularis oculi, procerus muscle, a corrugator supercilli and depressor anguli oris (see columns 6-7 and figure 1). Binder teaches that headaches may be associated with depression (column 1). Binder teaches that botulinum toxin when administered to patients with headaches is effective in reducing pain and symptoms associated with or the onset of headaches in mammals (see the Abstract). Binder teaches that botulinum toxin can be administered in a dose of up to about 1,000 units although individual dosages of about 15-30 units are preferred (columns 5-6). Binder teaches that botulinum toxin injection be effective up to about 3 to 6 months (column 7). Therefore the combination of prior art references teach the claim limitation "...further comprising administering an additional dose of 30-50 unit equivalents of botulinum A to the facial muscle after about two to six months".

Jahanshahi et al and Binder do not teach claim limitation "... affecting the ability of the subject to frown".

Carruthers et al teach that botulinum toxin can be used to cause paralysis to a depressor anguli oris in a patient to alleviate downturn at the corners of a patient's mouth (see the Abstract). Carruthers et al teach that this condition is called "sad mouth" column 2).

It would be *prima facie* obvious at the time the invention was made to administer botulinum toxin to patients suffering from depression as well as affecting the ability of the patient to frown or scowl because Jahanshahi et al teach that administering botulinum toxin to torticollis patients experiencing depression significantly reduced

levels of depression and anxiety, Binder teaches that botulinum toxin can be effectively administered to facial muscles such as the frontalis, orbicularis oculi, procerus muscle, a corrugator supercilli and depressor anguli oris and Carruthers et al teach that botulinum toxin can be used to cause paralysis to a depressor anguli oris in a patient to alleviate downturn at the corners of a patient's mouth. Based on the teachings of the combined prior art references, it would be expected barring evidence to the contrary, that the administration of botulinum toxin to the facial muscles of patients suffering from depression would be an effective way to treat depression as well as anxiety in these patients.

Applicant's Arguments

A. Applicant urges that the Office allegation that Jahanshahi et al teach alleviation of depression using botulinum toxin is incorrect.

Applicant urges that Jahanshahi et al teach selection of subject with torticollis.

Applicant urges that Binder et al suggest the selection of a subject with a headache. Binder et al teach that headaches can be associated with headaches.

Applicant urges that Carruthers et al teach selecting a subject for cosmetic use of botulinum toxin.

Applicant urges that neither Jahanshahi et al , Binder et al or Carruthers et al suggest or render obvious "selecting a subject diagnosed with major depression or dysthymia".

B. Applicant urges that the Examiner's reference to transitional language, "comprising" in the claims is misplaced.

C. Applicant urges that the Office discounts the Declaration of Dr. Capehart. Applicant urges that in his declaration Dr. Capehart confirmed that Jahanshahi et al does not suggest to be a psychiatrist that botulinum toxin should be used to treat depression in the absence of underlying torticollis. Applicant urges that Dr. Capehart provided the information that the innervation of the neck is through the spinal root of the accessory nerve (CN XI) and branches of the second and third cervical nerves. Applicant urges that the declaration set forth the scientific basis supporting the assertion that the claimed invention would not be obvious to one of ordinary skill in the art, based on any of the prior art of record. Applicant urges that the confirmed that a psychiatrist would look to a therapeutic modality for torticollis to treat major depression nor would they look at headache medications to provide a route of administration for a psychiatric disorder such as major depression.

D. Applicant urges that Jahanshahi et al teach the evaluation of patients with torticollis using the Beck Depression Inventory, which is used to evaluate depressive symptoms in a variety of subjects. Applicant urges that the Beck Depression Inventory is a well-known method of evaluating clinical criteria. Applicant urges that the Beck Depression Inventory would not suggest to a psychiatrist to use a therapeutic modality for torticollis to treat major depression nor would they look to headache medications to provide a route of administration for a psychiatric disorder.

E. Applicant urges that the Office discounts the Declaration of Dr. Finzi which provided evidence of unexpected superior results of the claimed invention. Applicant urges that they are unaware of any requirement to provide the location wherein studies were conducted. Applicant urges that the claims are limited to methods for treating depression that include the injection of a neurotoxin into the corrugator supercilii or the procerus muscle. Applicant urges that Dr. Finzi compared the effect of the injection of botulinum toxin into different muscles of the face for treating depression. Applicant urges that the specification discloses three patients which are treated for depression using the method of the claimed invention. Applicant urges that unexpected superior results obtained by using the claimed methods overcome any prima facie case of obviousness.

Examiner's Response to Applicant's Arguments

Applicant's arguments filed January 2, 2009 have been fully considered but they are not persuasive.

A) It should be noted that the claimed method is directed to treating major depression or dysthymia or primary intermittent anxiety comprising selecting a subject diagnosed with major depression or dysthymia or primary intermittent anxiety. The claims are not limited to patients that only suffer from major depression or dysthymia or primary intermittent anxiety since open transitional claim language such as "comprising" is recited in the claimed method. See MPEP 2111 for Transitional Language. Thus,

the population of patients taught in Jahanshahi et al fall within the scope of the patients used in the claimed method.

Jahanshahi et al teach a method of treating patients suffering from torticollis as well as depression (e.g. psychological functioning) before and after administration of botulinum toxin. These patients were evaluated using The Beck Depression Inventory, (see Jahanshahi et al page 230, 1st column) which meet the claim limitation "...using specific clinical criteria for major depression or dysthymia or primary intermittent anxiety...". It should be noted that the instant specification at page 13 confirms that this inventory should be used when evaluating patients for depression. Jahanshahi et al teach that in this study there was a significant improvement in depression of patients that received botulinum toxin injections (page 231). *The prior art teaches success in reducing in depression patients by administering botulinum toxin.*

Binder teaches that botulinum toxin can be administered to various muscles in the face and head including the frontalis, orbicularis oculi, procerus muscle, a corrugator supercilli and depressor anguli oris (see columns 6-7 and figure 1). Binder teaches that headaches may be associated with depression (column 1). *The prior art has demonstrated success with administering botulinum toxin to the procerus muscle or a corrugator supercilli muscle.*

Carruthers et al teach that botulinum toxin can be used to cause paralysis to a depressor anguli oris in a patient to alleviate downturn at the corners of a patient's mouth (see the Abstract). Carruthers et al teach that this condition is called "sad

mouth" column 2). *The prior art teaches success when administering botulinum toxin to achieve a predictable outcome, "frowning or appearing sad".*

Therefore, it would be obvious to one of ordinary skill that the combination of prior art references as combined provided a *prima facie* case of obviousness because it is obvious to combination familiar elements (techniques) according to known methods when it does no more than yield predictable results. The combination of prior art references teach the claimed invention absent convincing evidence to the contrary.

The Examiner disagrees that with Applicant's assertion that the combination of references would not lead the artisan of ordinary skill to the route of administering botulinum toxin to the corrugator supercilii or procerus muscles. As stated above, Binder teaches that botulinum toxin can be administered to various muscles in the face and head including the frontalis, orbicularis oculi, procerus muscle, a corrugator supercilli and depressor anguli oris (see columns 6-7 and figure 1). Binder teaches that headaches may be associated with depression (column 1). Thus, the artisan of ordinary skill would reasonably conclude that one could administer botulinum toxin to head and facial muscles treat headaches as well as depression.

B) To address Applicant comment regarding transitional language, the claims recite the transitional language "comprising". Comprising is open-ended language and does not exclude populations of patients that have other disorders such as torticollis or headaches as well as suffering from depression.

C) To address the Declaration of Dr. Capehart filed under 37 CFR 1.132, it should be noted that this declaration is insufficient to overcome the rejection of claims 1-15 and 23 and 24 as set forth in the last Office action. It should be noted that Dr. Capehart makes an assertion in his declaration that Jahanshahi et al does not suggest to a psychiatrist that botulinum toxin should be used to treat depression in the absence of underlying torticollis. To address Dr, Capehart's comments regarding physician's understanding of anatomy and physiology would not predict that injections of botulinum toxin into the neck to have the same effect as injection of botulinum toxin into the corrugator supercilli or procerus muscle, it should be noted that the outcome of the method taught by Jahanshahi et al is that there was a significant improvement in depression (page 231, 1st column). Jahanshahi et al teach that reduction of depression and disability were major psychological benefits of the botulinum toxin injections (page 231, 1st column). As stated above, the pending claims do not exclude patients that have other disorders as well as suffering from major depression.

D) To address Applicant's comments regarding The Beck Depression Inventory, Jahanshahi et al teach that patients were evaluated using The Beck Depression Inventory, (see Jahanshahi et al page 230, 1st column) which meet the claim limitation "...using specific clinical criteria for major depression or dysthymia or primary intermittent anxiety...". It should be noted that the instant specification at page 13 confirms that this inventory should be used when evaluating patients for depression.

E) To address the Declaration of Dr. Finzi filed under 37 CFR 1.132, it should be noted that this declaration is insufficient to overcome the rejection of claims 1, 4-8, 12-21 and 23-24 as set forth in the last Office action. To address Dr Finzi comments regarding unexpected superior results, the submission of the objective evidence of patentability does not mandate a conclusion of patentability. See In re Payne, 606 F.2d. 303, 203 USPQ 245 (CCPA 1979). The combination of prior art references teach injection of botulinum toxin into the corrugator supercilli or the procerus muscle leads to effective results. The prior art has demonstrated success with administering botulinum toxin to the procerus muscle or a corrugator supercilli muscle. Additionally, MPEP 2141, *KSR International Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1741 (2007), discloses that if a technique has been used to improve one method , and a person of ordinary skill would recognize that it would be used in similar methods in the same way, using the technique is obvious unless its application is beyond that person's skill. *KSR International Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1741 (2007) also discloses that "The combination of familiar element according to known methods is likely to be obvious when it does no more than yield predictable results". Based on the rejection as combined above, it would be obvious to apply a known technique to a known product to be used in a known method that is ready for improvement to yield predictable results.

To address the data disclosed in the Declaration of Dr. Finzi, it should be noted although the record may establish evidence of secondary considerations which are indicia of nonobviousness, the record may also establish such a strong case of

obviousness that the objective evidence of nonobviousness is not sufficient to outweigh the evidence of obviousness. Newell Cos. v. Kenney Mfg. Co., 864 F.2d 757, 769, 9 USPQ2d 1417, 1427 (Fed. Cir. 1988), cert. denied, 493 U.S. 814 (1989); Richardson-Vicks, Inc., v. The Upjohn Co., 122 F.3d 1476, 1484, 44 USPQ2d 1181, 1187 (Fed. Cir. 1997). See MPE P 716.01.

In view of all of the above, this rejection is maintained.

4. The rejection under 35 U.S.C. 103(a) is maintained for claims 16-21 for the reasons set forth on pages 7-10, paragraph 4 of the Final Office Action. The rejection is reiterated below:

The rejection was on the grounds that the teaching of Jahanshahi et al, Binder and Carruthers et al as applied to claims 1-15, 22 and 23-24 above and further in view of Wagstaff et al *(Drugs 2002;62(4):655-703)(Abstract only)*.

Jahanshahi et al, Binder and Carruthers et al have been described previously.

Jahanshahi et al, Binder and Carruthers et al do not teach an additional modality of treatment for depression.

Wagstaff et al teach that paroxetine is a selective serotonin reuptake inhibitor (SSRI) with antidepressant and anxiolytic activity (see the Abstract). Wagstaff et al teach that paroxetine is effective at treating depressive disorder (see the Abstract). Wagstaff et al teach that the common adverse effects with using paroxetine include headache (see the Abstract). Wagstaff et al teach that paroxetine is an important first-line option for treatment of major depressive disorder, obsessive-compulsive disorder, panic disorder, social anxiety disorder, general anxiety disorder and post-traumatic stress disorder (see the Abstract).

It would be *prima facie* obvious at the time the invention was made to use an additional modality of treatment for depression such as administration of SSRIs to patients suffering from depression because Jahanshahi et al suggest that use of other concepts may be helpful with direct management of psychological aspects such as body concept and low self-esteem. One of ordinary skill in the art would be motivated to administer SSRIs to treat patients with torticollis who suffer from depression because Jahanshahi et al has demonstrated that these patients experience psychological aspects such as body concept and low self-esteem even after botulinum toxin treatment. Therefore, one of skill in the art would reasonably conclude that the addition of a SSRI such as paroxetine would be effective at treating these patients since

Wagstaff et al teach that paroxtine is effective in treating depressive disorders such as social anxiety disorder and general anxiety disorder. Based on the teachings of the combined prior art references, it would be expected barring evidence to the contrary, that the administration of botulinum toxin and a SSRI to patients suffering from depression would be effective in treating depression.

Applicant's Arguments

A) Applicant urges that SSRIs are not used to treat the muscle spasms of torticollis or headaches and are not used for cosmetic purposes. Applicant urges that with regard to torticollis, Kaplan & Saddock's Pocket Handbook of Clinical Psychiatry discloses that one of the side effects of selective serotonin reuptake inhibitors is that they can cause torticollis.

B) Applicant urges that the Office does not properly address the Diller et al reference. Diller et al disclose that a patient taking fluoxetine developed torticollis. Applicant asserts that SSRIs can cause torticollis and is not specific to fluoxetine. Applicant urges that one of skill in the art would understand Diller et al to teach away form the use of any SSRI in torticollis. Applicant urges based on the specification and the Declarations of record overcomes any prima face case of obviousness.

Examiner's Response to Applicant's Arguments

Applicant's arguments filed January 2, 2009 have been fully considered but they are not persuasive.

A) The examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references

themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In the instant case, one of ordinary skill would be motivated to use botulinum toxin to administer SSRIs to treat patients who suffer from depression because Jahanshahi et al has demonstrated that these patients experience psychological aspects such as body concept and low self-esteem even after botulinum toxin treatment. Therefore, one of skill in the art would reasonably conclude that the addition of a SSRI such as paroxetine would be effective at treating these patients since Wagstaff et al teach that paroxtine is effective in treating depressive disorders such as social anxiety disorder and general anxiety disorder. Based on the teachings of the combined prior art references, it would be expected barring evidence to the contrary, that the administration of botulinum toxin and a SSRI to patients suffering from depression would be effective in treating depression.

B) To address Applicant's comment's regarding paroxetine causing torticollis, it should be noted that the patient in this case was being treated with fluoxetine and benztropine and not specifically, paroxetine. The Abstract of Diller et al provided by Applicant does not indicate that paroxetine alone caused the development of torticollis. It may have been a synergistic effect with the combination of drugs administered. It should be noted that Diller et al teach fluoxetine and benztropine specifically caused torticollis in a 15 year old girl. Diller et al disclose one case, in particular one youth patient that developed torticollis after treatment with fluoxetine and benztropine. Diller et al is silent as to if these specific drugs can cause torticollis in other populations of

patients such as adults. Based on the teachings of Wagastaff et al SSRI are very effective in treating patients that suffer from depression as well as dysthymia. Thus, in the event that SSRIs caused any side effects such as torticollis in certain patients, it should be noted that botulinum toxin can be used to treat depression as well as torticollis. The combination of prior art references teach the claimed invention.

In view of all of the above, this rejection is maintained.

5. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Status of Claims

6. No claims allowed.

Conclusion

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Vanessa L. Ford whose telephone number is (571) 272-0857. The examiner can normally be reached on 9 am- 6 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert Mondesi can be reached on (571) 272-0856. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Vanessa L. Ford/
Examiner, Art Unit 1645
April 10, 2009

/Robert B Mondesi/
Supervisory Patent Examiner, Art Unit 1645